

REMARKS

Claims 41, 46, 51 and 56 are currently amended. New claim 58 is added. Reconsideration is urged.

I. The rejection of claims 46, 51 and 56 under 35 U.S.C. 112, second paragraph

Claims 46, 51 and 56 are currently amended. Reconsideration is urged.

II. The rejection of claims 41 and 46-49 under 35 U.S.C. 102(e)

Claims 41 and 46-49 stand rejected as anticipated by Andersen et al (US Patent Publication No. 2003/0129718) hereinafter referred to simply as "Andersen".

Claim 41, as currently amended, requires, a variant of an alpha-amylase, the variant including an amino acid sequence having at least 90% homology to SEQ ID NO:8, including an alteration at a position corresponding to position K170 in SEQ ID NO:8, and including an alteration at one or more positions selected from the group of 49, 60, 104, 132, 161, 176, 179, 180, 181, 183, 200, 203, 204, 207, 212, 237, 239, 250, 280, 298, 318, 374, 385, 393, 402, 406, 427, 430, 440, 444, 447, and 482 (using SEQ ID NO:8 for numbering), and wherein the variant has alpha-amylase activity. In other words, at least 90% identity to SEQ ID NO:8, modification at K170, and the claimed combination of alterations is required. Andersen does not show each and every limitation. The Examiner has erred by referring to the AA560 amylase for support in this rejection. See for example, paragraph 390 of Andersen which refers to a number of positions of the AA560 amylase. According to Table 1 of both the instant specification and Table 1 of Andersen, AA560 and TERMAMYL brand amylase share 68.3 % identity. Thus, Anderson does not show the claimed combination of alterations including 90% homology. Reconsideration is urged.

Claims 46 through 49 depend on Claim 41 and are not anticipated for the same reasons that Claim 41 is not anticipated.

III. The rejection of claims 41, 44 and 46-49 under 35 U.S.C. 102(b)

Claims 41, 44 and 46-49 stand rejected as anticipated by Borchert (WO 99/23211) hereinafter referred to simply as "Borchert".

Claim 41, as currently amended, requires, a variant of an alpha-amylase, the variant including an amino acid sequence having at least 90% homology to SEQ ID NO:8, including an alteration at a position corresponding to position K170 in SEQ ID NO:8, and including an

alteration at one or more positions selected from the group of 49, 60, 104, 132, 161, 176, 179, 180, 181, 183, 200, 203, 204, 207, 212, 237, 239, 250, 280, 298, 318, 374, 385, 393, 402, 406, 427, 430, 440, 444, 447, and 482 (using SEQ ID NO:8 for numbering), and wherein the variant has alpha-amylase activity. In other words, at least 90% identity to SEQ ID NO:8, modification at K170, and the claimed combination of alterations is required. Borchert does not show each and every limitation. The Examiner has erred by referring to the SP722 amylase for support in this rejection. According to Table 1 of both the instant specification, SP722 and TERMAMYL brand amylase share 70.8 % identity. Thus, Borchert does not show the claimed combination of alterations including 90% homology. Reconsideration is urged.

Claims 44, 46 through 49 depend on Claim 41 and are not anticipated for the same reasons that Claim 41 is not anticipated.

IV. The Rejection of claims 43, 51-56 under 103(a)

Claims 43 and 51-56 stand rejected as obvious in light of Andersen.

Initially, Applicants note that claim 43 depends upon claim 41. As Claim 41 is not considered obvious by the Examiner, Claim 43 is not obvious for the same reasons. Further, as explained above, Andersen fails to show each and every element of claim 41. Accordingly, Andersen fails to show each and every element of claim 43. Reconsideration is urged.

The present disclosure relates to specified variants of parent Termamyl-like alpha amylases which variants have alpha-amylase activities and exhibit an alteration in various properties such as excellent stability at higher temperature or low pH conditions.

Claim 51, requires, a variant of an alpha-amylase, wherein the variant comprises an amino acid sequence having at least 90% homology to SEQ ID NO.8 and a substitution of the residue at a position corresponding to position 170 in SEQ ID NO:8 with a Q residue, and wherein the variant has alpha-amylase activity.

Claim 56, as amended, requires a variant *Bacillus licheniformis* alpha-amylase, wherein the variant includes an amino acid sequence having at least 90% homology to SEQ ID NO:8 and a substitution of the residue at position corresponding to position 170 in SEQ ID NO:8 with a Q residue, and wherein the variant has alpha-amylase activity.

A patent claim is obvious over a combination of prior art references only when “the prior art would have suggested to one of ordinary skill in the art that [the claimed invention] should be carried out and would have a reasonable likelihood of success... . Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant’s disclosure.” *In re*

Dow Chemical, 837 F.2d 469, 473 (Fed. Cir. 1988); see also, 35 U.S.C. § 103. An invitation to experiment, alone, cannot make an invention obvious. *In re Dow*, 837 F.2d at 473.

Applicants believe there is no evidence given by Andersen that an alpha-amylase that does not natively have a "Q" at position 170 could be modified to include a "Q" at this position to successfully create a variant in accordance with the present disclosure. A skilled person in the art would have no reasonable expectation of success that changing position 170 to a Q in sequences having 90% homology to SEQ ID NO: 8 would solve the problems of the present disclosure. Even if it was obvious to try to experiment it is not necessarily true that there would be any reasonable expectation of success. With respect to claims 51 and 56, a reasonable expectation of success requires that the skilled person can predict that substitution of the residue at position corresponding to position 170 in SEQ ID NO:8 with a Q residue would result in an enzyme having alpha-amylase activity in accordance with the present disclosure.

The cited reference is devoid of any suggestion to make the specified alpha-amylases, as advanced by the Examiner, except from using Applicants' disclosure as a template through hindsight reconstruction of Applicants' claim. Thus, the Examiner has erroneously retraced the path of the inventor with hindsight --discounting the number of complexities of the alternatives in order to conclude that the specifically claimed composition was obvious. This reasoning is always inappropriate for an obviousness test based on the language of Title 35 that requires the analysis to examine "the subject matter as a whole" to ascertain if it "would have been obvious at the time the invention was made." 35 U.S.C. § 103(a).

Applying a non-rigid TSM analysis, a wild-type "Q" in a specific position would not give the skilled person motivation to mutate a corresponding position in other alpha-amylases. Thus, one of skill in the art would not be motivated to alter an alpha-amylase not having a "Q" at position 170 to include a Q and arrive at Applicants' claimed invention. For example, one of ordinary skill in the art would not be not be motivated to alter an alpha-amylase having a "K" at position 170 to include a Q and arrive at Applicants' invention.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 103, and claims 43, 51 and 56 are not obvious. Applicants respectfully request reconsideration and withdrawal of the rejection.

V. The Rejection of claims 41, 44 and 46-49 under 103(a)

Claims 41, 44 and 46-49 stand rejected as obvious in light of Borchert in view of Andersen (U.S. 6,410,295) hereinafter referred to as "Andersen II".

As explained above, Borchert does not show the claimed combination of alterations including 90% homology. The Examiner now offers Andersen II in an attempt to cure the deficiencies of Borchert. While, Andersen II relates to novel variants of parent Termamyl-like alpha amylases, it does not cure the deficiencies of Borchert.

More specifically, Claim 41, as amended, requires a variant of an alpha-amylase, the variant including an amino acid sequence having at least 90% homology to SEQ ID NO:8, including an alteration at a position corresponding to position K170 in SEQ ID NO:8, and including an alteration at one or more positions selected from the group of 49, 60, 104, 132, 161, 176, 179, 180, 181, 183, 200, 203, 204, 207, 212, 237, 239, 250, 280, 298, 318, 374, 385, 393, 402, 406, 427, 430, 440, 444, 447, and 482 (using SEQ ID NO:8 for numbering), and wherein the variant has alpha-amylase activity.

A patent claim is obvious over a combination of prior art references only when “the prior art would have suggested to one of ordinary skill in the art that [the claimed invention] should be carried out and would have a reasonable likelihood of success... . Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant’s disclosure.” *In re Dow Chemical*, 837 F.2d 469, 473 (Fed. Cir. 1988); see also, 35 U.S.C. § 103. An invitation to experiment, alone, cannot make an invention obvious. *In re Dow*, 837 F.2d at 473.

Applicants believe there is no evidence given by Borchert or Andersen II that an amino acid sequence having at least 90% homology to SEQ ID NO:8, including an alteration at a position corresponding to position K170 in SEQ ID NO:8, and including an alteration at one or more of the specified positions (using SEQ ID NO:8 for numbering), would have alpha-amylase activity in accordance with the present disclosure. A skilled person in the art would have no reasonable expectation of success that changing position K170 in sequences having 90% homology to SEQ ID NO: 8 would solve the problems of the present disclosure. Even if it was obvious to try to experiment it is not necessarily true that there would be any reasonable expectation of success. With respect to claim 41, a reasonable expectation of success requires that the skilled person can predict that substitution K170 in SEQ ID NO:8 would result in an enzyme having alpha-amylase activity in accordance with the present disclosure.

The cited references are devoid of any suggestion to make the specified alpha-amylase, as advanced by the Examiner, except from using Applicants' disclosure as a template through hindsight reconstruction of Applicants' claim. Thus, the Examiner has erroneously retraced the path of the inventor with hindsight --discounting the number of complexities of the alternatives in order to conclude that the specifically claimed composition was obvious. This reasoning is always inappropriate for an obviousness test based on the language of Title 35 that requires the

analysis to examine "the subject matter as a whole" to ascertain if it "would have been obvious at the time the invention was made." 35 U.S.C. § 103(a).

Applying a non-rigid TSM analysis, one of ordinary skill in the art would not be motivated to mutate the alpha-amylases of Borchert and Anderson II to somehow arrive at the Applicants' specifically claimed alpha-amylases.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 103. Applicants respectfully request reconsideration and withdrawal of the rejection.

VI. The Rejection of claims 41, 43, 44, 46-49 and 51-56 under 103(a)

Claims 41, 43, 44, 46-49 and 51-56 stand rejected as obvious in light of Andersen in view of Andersen II.

As explained above, Andersen is deficient and fails to disclose the claimed combination of alterations including 90% homology. The Examiner now cites Andersen II in an attempt to cure the obvious deficiencies of the reference. While, Andersen II relates to novel variants of parent Termamyl-like alpha amylases, it does not cure the deficiencies of Andersen.

The present disclosure relates to specified variants of parent Termamyl-like alpha amylases, which variant has alpha-amylase activities and exhibits an alteration in various properties such as excellent stability at higher temperature or low pH conditions.

Claim 41, as amended, requires a variant of an alpha-amylase, the variant including an amino acid sequence having at least 90% homology to SEQ ID NO:8, including an alteration at a position corresponding to position K170 in SEQ ID NO:8, and including an alteration at one or more positions selected from the group of 49, 60, 104, 132, 161, 176, 179, 180, 181, 183, 200, 203, 204, 207, 212, 237, 239, 250, 280, 298, 318, 374, 385, 393, 402, 406, 427, 430, 440, 444, 447, and 482 (using SEQ ID NO:8 for numbering), and wherein the variant has alpha-amylase activity.

Claim 51, as amended requires a variant of an alpha-amylase, wherein the variant comprises an amino acid sequence having at least 90% homology to SEQ ID NO:8 and a substitution of the residue at a position corresponding to position 170 in SEQ ID NO:8 with a Q residue, and wherein the variant has alpha-amylase activity.

Claim 56, as amended requires a variant *Bacillus licheniformis* alpha-amylase, wherein the variant comprises an amino acid sequence having at least 90% homology to SEQ ID NO:8 and a substitution of the residue at position corresponding to position 170 in SEQ ID NO:8 with a Q residue, and wherein the variant has alpha-amylase activity.

A patent claim is obvious over a combination of prior art references only when “the prior art would have suggested to one of ordinary skill in the art that [the claimed invention] should be carried out and would have a reasonable likelihood of success... . Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant’s disclosure.” *In re Dow Chemical*, 837 F.2d 469, 473 (Fed. Cir. 1988); see also, 35 U.S.C. § 103. An invitation to experiment, alone, cannot make an invention obvious. *In re Dow*, 837 F.2d at 473.

Applicants believe there is no evidence given by Andersen or Andersen II that an amino acid sequence having at least 90% homology to SEQ ID NO:8, including an alteration at a position corresponding to position K170 in SEQ ID NO:8, and including an alteration at one or more of the specified positions (using SEQ ID NO:8 for numbering), would have alpha-amylase activity in accordance with the present disclosure. A skilled person in the art would have no reasonable expectation of success that changing position K170 in sequences having 90% homology to SEQ ID NO: 8 would solve the problems of the present disclosure. Even if it was obvious to try to experiment it is not necessarily true that there would be any reasonable expectation of success. With respect to claims 41, 51 and 56 a reasonable expectation of success requires that the skilled person can predict that substitution K170 in SEQ ID NO:8 would result in an enzyme having alpha-amylase activity in accordance with the present disclosure.

The cited references are devoid of any suggestion to make the specified alpha-amylase, as advanced by the Examiner, except from using Applicants' disclosure as a template through hindsight reconstruction of Applicants' claim. Thus, the Examiner has erroneously retraced the path of the inventor with hindsight --discounting the number of complexities of the alternatives in order to conclude that the specifically claimed composition was obvious. This reasoning is always inappropriate for an obviousness test based on the language of Title 35 that requires the analysis to examine "the subject matter as a whole" to ascertain if it "would have been obvious at the time the invention was made." 35 U.S.C. § 103(a).

Applying a non-rigid TSM analysis, a wild-type "Q" in a specific position would not give the skilled person motivation to mutate a corresponding position in other alpha-amylases. Thus, one of skill in the art would not be motivated to alter an alpha-amylase not having a "Q" at position 170 to include a Q and arrive at Applicants' claimed invention. For example, one of ordinary skill in the art would not be not be motivated to alter an alpha-amylase having a "K" at position 170 to include a Q and arrive at Applicants' invention. One of ordinary skill in the art would not be motivated to mutate the alpha-amylases of Andersen and Anderson II to somehow arrive at the Applicants' specifically claimed alpha-amylases. Reconsideration is urged. No claim is obvious.

VII. New claim 58

Should any additional fees be due, the USPTO is authorized to charge deposit Account no. 50-1701. No new matter is added.

Respectfully submitted,

Date: March 16, 2009

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